Liver Dysfunction in Hypothyroid Non-Pregnant Women

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Abstract

Objective: To evaluate the effects of under secretion of thyroid hormones and its relation with liver markers i.e. alanine transaminase (ALT) and aspartate transaminase (AST) in non-pregnant women.
Methods: This cross-sectional study was conducted in Khyber Teaching Hospital Peshawar from March 2014 to March 2015. The study was performed on 150 non-pregnant women in the age group of 18-70, attending the outpatients departments of Khyber Teaching Hospital for thyroid screening. The exclusion criteria were pregnancy, hypertension, renal impairment and known history of liver abnormalities. Thyroid and liver function tests were performed for all the patients and control using standard kits and procedure. Normal subjects in the same age group were selected randomly from the local population of Peshawar city and were used as control (N) for the study. Competitive ELISA technique was used for the analysis of T3 and T4 on Dia 710 microplate reader, while sandwich ELISA was used for TSH analysis. Quantitative tests for both ALT and AST were performed according to the international federation of clinical chemist (IFCC) protocols on Erbamannhein chemistry auto-analyser (Germany) using standard Erba kits.
Results: ALT and AST level was found to be lower in the patient groups [Overtly hypothyroid (Oh): 24.35 ± 1.11 IU/L, sub-clinically hypothyroid (Sh): 16.85 ± 0.55 IU/L] than the control group (N: 29.69 ± 3.28 IU/L). A significant positive correlation was observed between AST and TSH (thyroid-stimulating hormone) in the control group (N) (p=0.002) and negative correlation in overtly hypothyroid (Oh) and sub-clinically hypothyroid (Sh) groups, respectively. No other significant correlation was observed between ALT, TSH, T3 (triiodothyronine) and T4 (thyroxine) in any other groups.
Conclusion: Both liver enzymes (ALT and AST) were found to be lower in the patients groups (Oh and Sh) as compared to control group (N).

Keywords: Hypothyroidism, alanine transaminase, aspartate transaminase, liver function test.
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Introduction

Thyroid hormones are involved in the regulation of basal metabolic rate of liver cells and bilirubin metabolism while liver is also involved in the regulation and metabolism of thyroid hormones[1-4]. Dysfunction of either organ may disturb the other. Liver enzymes are the biochemical markers used in assessing the liver health. The most widely used liver enzymes are the aminotransferases, which catalyse transamination reactions in the cells. These are enzymes, aspartate aminotransferase/serum glutamic oxaloacetate transaminase (AST/SGOT) and alanine aminotransferase/serum glutamic pyruvic transaminase (ALT/SGPT). Normal serum levels of AST and ALT are 5 to 40 Ù/L and 7 to 65 Ù/L, respectively. These enzymes are released into blood whenever the liver is damaged; the rise in the level of these enzymes in the blood is considered as a sign of liver damage. Abnormal levels of ALT and AST are most frequently observed in thyroid diseases which

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may lead to severe hepatocellular damage[5]. Flow of bile, bilirubin and bile salts also decreases in case of severe thyroidal dysfunction[6]. Both overt hypothyroidism (Oh) and sub-clinical hypothyroidism (Sh) are found to be associated with liver dysfunction and abnormal metabolism of lipoprotein.

The prevalence rate of thyroid dysfunctions is 10 times higher in women than men and its adverse effects in pregnant females are well-studied and established[7]. The prevalence rate of hypothyroidism is about 2.5% in normal pregnant women[8]. The World Health Organization (WHO) has reported the prevalence rate of goitre to be 22.2% in pregnant women (PW) and 20.9% in non-pregnant women (NPW). Iodine deficiency is reported in 2.5 billion people in world population, of which 313 million live in the South-Eastern Asian countries including Pakistan[9].

Iodine deficiency is a common health issue in northern Pakistan. The goitre prevalence is found to be 55% in the plains and 80-90% in the northern mountainous region[10,11]. As there is limited data on the effect of hypothyroidism on liver enzyme from Khyber Pakhtunkhwa, the present study was carriedto study the association of thyroid hypo-function with liver functions markers i.e. ALT and AST in NPW of Khyber Pakhtunkhwa.

Subjects and Methods

The present cross-sectional and analytical study was conducted in Khyber Teaching Hospital Peshawar in a one-year period (March 2014 to March 2015) on 150 non pregnant women hailing from different parts of Peshawar valley and its suburbs.The study was approved through letter no. 21876/KTH/P.S. by the ethical committee of the Khyber Teaching Hospital (KP). The data about age, weight, medical history and medication was collected on a data entry form from each patient on informed consent personally or through her attendant using purposive sampling methods. Subjects having pregnancy, hypertension, and renal diseases were excluded from the study. Patients consent was taken prior to sampling and explanation given for the objectives and outcome of the study. Approximately 2 mL of serum obtained from 5 mL of fresh blood sample of each patient was analysed for biochemical tests of thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), ALT and AST using standard kits and protocols.

Thyroid profile markers including TSH, T3 and T4 were determined by enzyme-linked immunosorbent assay (ELISA) methods using kits obtained from Biocheck (BC-1001, BC-1005 & BC-1007). Competitive ELISA technique was used for the analysis of T3 and T4 on Dia 710 micro plate reader (made in Australia)[12,13] while sandwich ELISA for TSH[14]. The normal ranges for TSH, T3 and T4 values were 0.4-6.0 µIU/mL, 0.6-1.85 ng/mL and 4.8-12.0 µg/dL, respectively.

Quantitative tests for both ALT and AST were performedaccording to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) protocols on Erbamannhein chemistry auto-analyser (Germany) using standard Erba kits[15].

The collected data was analysed on SPSS 17 software. Results were tabulated as mean ± SEM. Pearson's correlation and multiple linear regression analysis were also applied to the data to test for the association and dependency between the desired parameters. A p-value <0.05 was taken as of statistical significance.

Results

Table 1 shows the mean values of age, TSH, T3, T4, ALT and AST of the study population.The mean age of subjects in the control group (N), overtly hypothyroid (Oh) and sub-clinically hypothyroid (Sh), was 42.15 ± 1.86, 46 ± 18 and 45.97 ± 1.93 years, respectively. Mean value of serum TSH was found highest in the Oh group (25.89 ± 2.86 µIU/mL) and lowest in N group (2.38 ± 0.49 µIU/mL) while T3 and T4 values were higher in N than the other groups (T3:1.68 ± 0.005 ng/mL,T4:8.50 ± 1.59 µg/dL) and lowest in Oh group (T3: 0.94 ± 0.09 ng/mL, T4: 4.30 ± 0.28 µg/dL). The mean value of serum ALT and AST level was highest in N group (ALT: 26.69 ± 3.28 IU/L, AST: 33.70 ± 5.12 IU/L) and lowest in the Sh group (ALT: 16.85 ± 0.5I U/L, AST: 17.86 ± 0.98 IU/L).

Table 1. Comparison of age, TSH, T3, T4 ALT and AST of the study population

S no	Group ID	(n)	Mean age ± SE	Thyroid function markers			Liver function marker	
				TSH (5-45 IU/L)	T3 (5-45 IU/L)	T4	ALT	AST
1	N	54	42.15 ± 1.86	2.38 ± 0.49	1.68 ± 0.05	8.50 ± 1.59	29.6 ± 3.28	33.70 ± 5.12
2	Oh	48	46 ± 18	25.89 ± 2.86	0.94 ± 0.09	4.30 ± 028	24.35 ± 1.11	23.65 ± 1.22
3	Sh	48	45.97 ± 1.93	19.04 ± 2.22	1.47 ± 0.08	7.07 ± 0.38	16.85 ± 0.55	17.86 ± 0.98

n: frequency, N: Normal, Oh: Overtly hypothyroid, Sh: Subclinically hypothyroid, TSH: Thyroid-Stimulating Hormone, T3: Triiodothyronine, T4: Thyroxine, ALT: Alanine Transaminase, AST: Aspartate Transaminase, SEM: Standard Error of Means

Results of multiple linear regression analysis[16] using TSH, T3 and T4 as independent variable while ALT and AST as dependent variable, are given in Table 2. Positive relation was found for both ALT and AST with TSH and T3 while a negative relation with T4 was found in N group. In Oh group positive relation for ALT with TSH and T3 and negative withT4 was observed. Positive relation for ALT with TSH and T4 and negative with T3 in Shwas observed while AST had a negative relationwith TSH, T3 and T4 in both patients group (Oh and Sh).

Table 2. Multiple linear regression analysis of TSH, T3, T4, ALT and AST in N

	Model		Unstandardised coefficients (B)			
	DV		ALT		AST	
N			B	SE	B	SE
	Constant		30.16	23.11	28.56	13.33
		TSH	4.00	2.60	5.00	1.50
		T3	10.40	9.20	4.00	5.30
	IV	T4	-3.00	2.10	-1.80	1.20
	Constant		25.28	4.00	27.00	4.38
Oh		TSH	0.01	0.10	-0.10	0.10
	IV	T3	0.60	1.90	-1.20	2.10
		T4	-0.40	0.70	-0.20	0.70
Sh	Constant		17.03	2.83	22.30	5.01
	IV	TSH	0.01	0.10	-0.10	0.10
		T3	-1.10	1.20	-1.80	2.10
		T4	0.20	0.30	-0.10	0.40

DV: Dependent Variable, IV: Independent Variable, SE: Standard Error

The results of Pearson's Correlation analysis[17] are given in Table 3. Insignificant positive correlation for ALT with TSH in the entire study group was observed. In the N group,a very significant positive correlation was observed between AST and TSH (p=0.002). Insignificant negative correlation for AST with TSH was found in both Oh and Sh groups.

Insignificant positive correlation for ALT with T3 in N, Oh and negative in Sh group was found. Similarly, AST was found to have positive correlation with T3 in N and negative correlation in Oh and Sh groups, respectively. ALT showed insignificant correlation with T4 in N and Oh groups and positive in Sh while negative correlation with T4 in all the study groups.

Table 3. Correlation analysis of ALT and AST with TSH, T3 and T4 in the study population

Parameter	Group ID	Liver markers			
		ALT		AST	
		r	P	r	P
TSH	N	0.20	0.20	0.41**	0.00
	Oh	0.04	0.80	-0.10	0.60
	Sh	0.10	0.70	-0.60	0.70
T3	N	0.30	0.05	0.10	0.70
	Oh	0.03	0.80	-0.10	0.60
	Sh	-0.10	0.40	-0.10	0.60
T4	N	-0.20n	0.20	-0.20	0.20
	Oh	-0.10	0.60	-0.04	0.80
	Sh	0.04	0.80	-0.03	0.80

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).

Discussion

Normal secretions of thyroid hormones are necessary for the normal functions of all vital organs of human body including liver. There is an intricate association between these two important organs of our body and the data presented here, reveals how a small alteration in the serum level of one marker of either thyroid or liver will affect the level of another marker in the study population. Our study population comprises of non-pregnant women (n= 150) in the age group of 18-75 years which were the newly diagnosed cases of thyroid hypo-functions hailing from different parts of Khyber Pakhtunkhwa in Pakistan.

We observed significance differences in the ALT and AST level in all the three groups of our study population. The level of ALT and AST in both Oh and Sh was lower than N group of the study population. Some earlier studies have reported that these enzymes may be elevatedin hypothyroid patients but these studies have not mentioned ethnicity, sex differences, geographical and genetic factors which may have influenced the results of our study population[18]. A few studies have reported decreased activity of UDP-glucuronyl transferase (uridine 5'-diphospho-glucuronyl transferase) in hypothyroid patients resulting in cholestatic jaundice and low excretion of bilirubin. Hypothyroidism has been associated with cholestatic jaundice. In one experiment-induced hypothyroidism, the activity of bilirubin UDP-glucuronyl transferase was found reduced, which resulted in the decreased excretion of bilirubin from the body[19]. The decrease in the flow of bile is the result of an increase in the ratio of membrane cholesterol and phospholipid and the decrease in the fluidity of the membrane which can affect a large number of membrane transporters and also a number of enzymes. Gallstones formation is encouraged in hypothyroid patients due to lowered bilirubin excretion, hypercholesterolemia and hypotonia of the gall bladder[20]. Recent reports have however indicated that the liver abnormalities caused by hypothyroidism can be reversed in a short time following therapy, with no residual hepatic damage[21].

Significant correlation was observed between AST and TSH in the N group (p=0.002), while insignificant negative correlation of AST and TSH was found in the Oh and Sh groups. AST was found to have insignificant negative correlation with T4 inall the three groups. No significant correlation was observed between ALT, TSH, T3 and T4 in any of the three groups. Other studies have also reported similar correlations between thyroid markers, gamma glutamyl transferase and ALT[22].

Iodine deficiency and thyroid dysfunction is a common problem in northern Pakistan affecting women more as compared to the other gender due to poverty, lack of education, social taboos and lack of health facilities in rural areas. Moreover, there is a lack of adequate amount of iodine in drinking water and iodized salt due to lack of strict quality control. Awareness program about the importance of dietary iodine may be inculcated among the general public. Also, primary screening of iodine deficiency in school-going children may be initiated to arrest the diseases in early stages and minimise the secondary complications associated with thyroid dysfunction. According to the best of our knowledge, no such paper has been found during our literature search from this area of Pakistan where the goitre prevalence is found to be 55% in the plains and 80-90% in the northern mountainous region[10,11].

The study has got a number of limitations which could not be ignored. The study was conducted in only one tertiary care hospital and hence, its results are not the true representations of the whole population. More over the study group comprised of only non-pregnant women excluding others and the sample size was too small consisting of only 150 NPW. The study group was mostly illiterate women, unable to communicate efficiently and hence, making the collection of authentic data pertaining to their medical history and age, difficult. The time constraint was another limitation of the study. Lastly, availability of finance was the major hurdle in widening the scope of the study. Further studies involving larger populations will yield good results for better understanding the complex relationship between thyroid and liver function in hypothyroid subjects.

Conclusion

Both liver enzymes (ALT and AST) were found to be lower in the patients groups, overtly hy-

pothyroid (Oh) and sub-clinically hypothyroid (Sh) as compared to control group (N). Our study reveals that there is a complex interdependency of thyroid gland and liver on each other, and a multi-system approach should be adopted while treating patients with diseases affecting either organ.

Conflict of Interest

Authors have no conflict of interests and no grant/funding from any organisation.

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